

# Bioceramics: Materials *and* Applications



*Edited by*

Gary Fischman  
Alfred University

Alexis Clare  
Alfred University

Larry Hench  
University of Florida



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# EFFECTS OF SULFATE IONS ON THE *IN VITRO* PROPERTIES OF $\beta$ -TCP - MCPM - WATER MIXTURES. PRELIMINARY *IN VIVO* RESULTS

M. Bohner\*<sup>1#</sup>, J. Lemaître<sup>1</sup>, K. Ohura<sup>2</sup>, P. Hardouin<sup>2</sup>

<sup>1</sup>Laboratory of Powder Technology (LTP), DMX, EPFL, CH-1015 Lausanne, Switzerland; <sup>2</sup>Institut Calot, 62608 Berck-Sur-Mer, France.

# Present address: Center for Biopolymers at Interfaces, Dept. of Chem. and Fuel Engineering, Merrill Engineering building, University of Utah, Salt Lake City, Utah 84112.

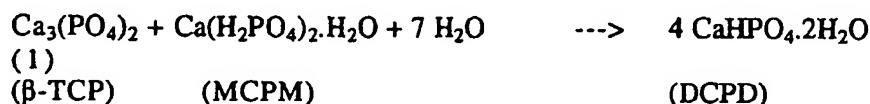
Five different sulfate compounds were used in order to assess the effects of sulfate ions on the *in vitro* properties of  $\beta$ -tricalcium phosphate ( $\beta$ -TCP) - monocalcium phosphate monohydrate (MCPM) - water mixtures.

A 0.1 M sulfate concentration doubles the setting time. This is attributed to the inhibitory effect of these ions on the growth of dicalcium phosphate dihydrate (DCPD), the product of the setting reaction. Increasing the sulfate concentration above 0.1 M results in a sharp decrease of the setting time and the DCPD crystal size, and a concomitant increase of the tensile strength. These phenomena are ascribed to the precipitation of calcium sulfate dihydrate crystals (CSD) which then act as heterogeneous nuclei for the growth of DCPD.

Cement cylinders made of  $\beta$ -TCP - MCPM -  $\text{CaSO}_4 \cdot 1/2\text{H}_2\text{O}$  (= CSH) -  $\text{H}_2\text{O}$  mixtures were implanted into rabbit femora. Results show that the cement cylinders were almost totally resorbed and replaced by new bone after 8 weeks.

## 1. Introduction

A new calcium phosphate cement (CPC) was recently studied by Lemaître et al.<sup>1-6</sup>. This cement is made out of mixtures of  $\beta$ -tricalcium phosphate ( $\beta$ -TCP;  $\beta\text{-Ca}_3(\text{PO}_4)_2$ ), monocalcium phosphate monohydrate (MCPM;  $\text{Ca}(\text{H}_2\text{PO}_4)_2 \cdot \text{H}_2\text{O}$ ) and water. The setting reaction can be written:



An implantation study of this cement in the long bones of mongrel dogs has shown that it is biodegradable and osteoconductive<sup>5</sup>. Therefore, this new CPC could potentially be used in the repair of bone defects in the human body, for example as a reinforcement material for osteoporotic bones<sup>6</sup>. However, for this purpose, the plasticity and the setting time of

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the cement's paste, as well as the mechanical strength of the hardened cement must match the needs of surgeons. Unfortunately, the setting time (30") and the tensile strength (1.2 MPa) of the cements made of  $\beta$ -TCP - MCPM -  $H_2O$  mixtures are low<sup>2</sup>. As a comparison, the tensile strength of the cortical bone is in between 50 and 150 MPa<sup>7</sup>. In order to improve the poor physico-chemical properties of this kind of cement, several additives can be used<sup>2</sup>: calcium pyrophosphate (CPP;  $Ca_2P_2O_7$ ), calcium sulfate hemihydrate (CSH;  $CaSO_4 \cdot 1/2H_2O$ ) or calcium sulfate dihydrate (CSD;  $CaSO_4 \cdot 2H_2O$ ). When 10 to 20 weight percents of CPP, CSH or CSD are added to the basic composition, the setting time increases from ten to twenty times. At the same time, CSH doubles the tensile strength, meanwhile CPP and CSD do not modify it. The effects of these additives have not been explained by Mirtchi and al.<sup>2</sup>. However, a good comprehension of the setting processes are compulsory in order to reach a good control of the physico-chemical properties of the cement. This study is therefore devoted to the understanding of the effects of sulfate ions.

## 2. Experimental

### 2.1. Materials

CSH (Merck; art. 2162, N°726K00498762); Sodium sulfate decahydrated (SSDH;  $Na_2SO_4 \cdot 10H_2O$  Merck; art 6648, N°510TA788548); Potassium sulfate (PS;  $K_2SO_4$  Merck; art. 527, N°527A955753); Magnesium sulfate heptahydrated (MSHH;  $MgSO_4 \cdot 7H_2O$  Alfa; art. 306066, N° 044780709); MCPM (Alfa; art. 304260, N°52701608).  $\beta$ -TCP prepared with equimolar amounts of dicalcium phosphate (DCP;  $CaHPO_4$  Merck; art. 2144, N°535K973044) and hydroxyapatite (HAP;  $Ca_5(PO_4)_3OH$ ; Bioland; Toulouse, France). The powder was firstly mixed in a Turbula mixer (T2C) with 10 alumina balls (4 g each) at a speed of 42 rpm for 30 minutes. Then the powder was calcined at 1100°C for 4 hours in dry air. After cooling down the partially sintered powder was ground until everything could pass through a 250  $\mu m$  sieve. Finally, the powder was homogeneized using the Turbula mixer for 30 minutes at 42 RPM.

### 2.2. Sample preparation

The MCPM powder, the sulfate compound and the deionized water were mixed together with a pestle and a mortar for 30 seconds. Then, the  $\beta$ -TCP powder was added and the paste was mixed with a spatula for 60 seconds. Afterwards, the paste was filled into syringes (diameter 12.5 mm) and setting time measurements were performed. The time zero corresponded to the moment when the  $\beta$ -TCP powder was added. After hardening, the sample was removed from the mould, put into a polystyrene box filled with 2 ml of deionized water and aged for 24

hours. Later on, the sample was dried in air at room temperature until a constant weight was reached. Each sample contained 1.6 g of  $\beta$ -TCP and usually 0.5 g of MCPM. 0.5 ml of water was added per gram of cement powder, except for CSH which needed more water (0.65 ml/g). With sulfuric acid, a constant amount of solution was used (1.26 ml). Usually, three samples were prepared for each composition.

### 2.3. Characterizations

The samples were characterized with setting time, porosity and diametral tensile strength measurements. They were also observed by scanning electron microscopy (SEM) and analysed by X-ray diffraction (XRD). The procedures used are described elsewhere<sup>4,8</sup>.

The corrected tensile strength,  $\sigma_{\text{corr}}$ , of a sample was defined as the tensile strength of a zero-porosity sample and calculated by:  $\sigma_{\text{corr}} = \sigma / (1 - p^{1/3})(1 - p^{2/3})$ , where  $\sigma$  is the tensile strength and  $p$  is the porosity.

### 2.4. *In vivo* testing

Cylinders (diameter: 4.75 mm; length: 10 mm) made of 64% of  $\beta$ -TCP, 20% of MCPM and 16% of CSH (commercial formulation: Bionice<sup>TM</sup>; Bioland, Toulouse, France) were implanted into the created cavity in the distal femora epiphyses of rabbits (female, race New Zealand, 3.8 to 4.2 kg). The rabbits were sacrificed after 4, 8 and 16 weeks. The evolution of the resorption rate and the bone ingrowth was followed by taking micro-radiographies of the median sections of the cavities (histological sections, thickness: 100  $\mu\text{m}$ ).

For more details on the experimental part, see reference 4.

## 3. Results and discussion

The figure 1 represents the effect of PS, CSH, MSHH, and SSDH on the setting time of the cements. Except for CSH, all the sulfate compounds provoke two increases of the setting time: the first at a small weight fraction (around 2%), and the second at a high weight fraction (7 to 15%). If it is supposed that the sulfate compound dissolves completely in the mixing liquid, and if the weight fraction is transformed into a concentration, it can be seen that the two increases of the setting time happen at nearly the same concentration for all the sulfate compounds used (fig. 2a and 2b). These concentrations are around 0.1 M and 0.9 M. Therefore, the nature of the cation does not play any large role in the setting time. It is the concentration of sulfate ions in the solution which is responsible for the increase of the setting time. The effects of the sulfuric acid solution and CSH on setting time are shown in figure 2b. Sulfuric acid causes only the first increase of the setting time, while CSH provokes a steady but slow increase.

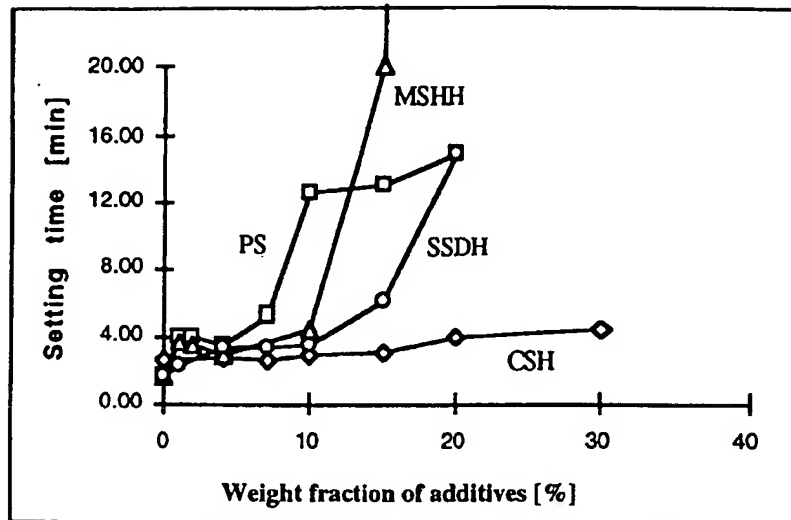


Fig. 1: Influence of several additives on the setting time of cements. Composition of the cements: 1.6 g of  $\beta$ -TCP, 0.5 g of MCPM, x g of sulfate compound and 0.5 ml/g of deionized water (0.65 ml/g for CSH).

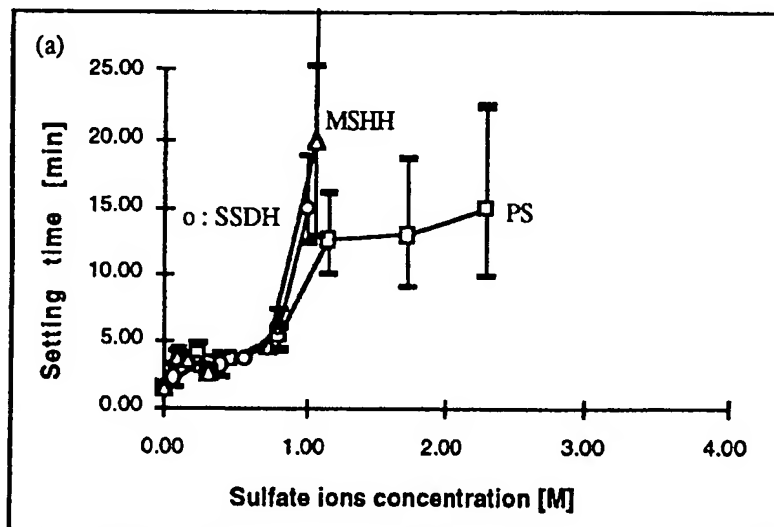


Fig. 2: time (Composition and 0.1 solution

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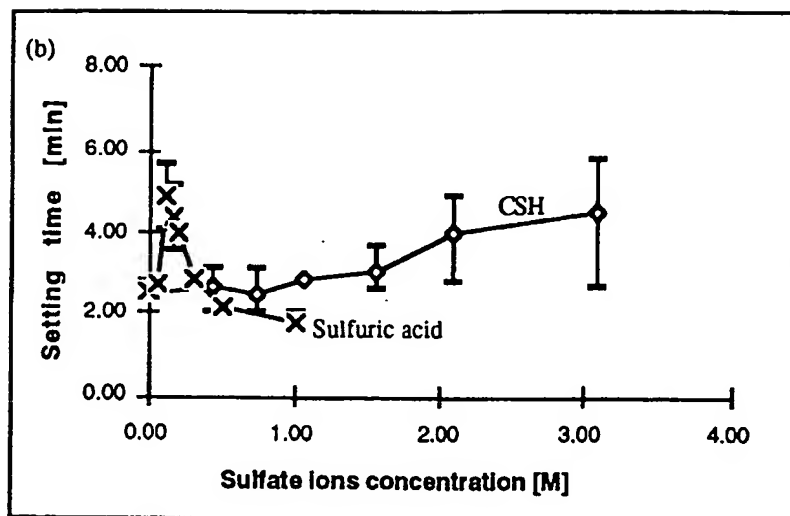


Fig. 2: Influence of the sulfate concentration in the mixing liquid on the setting time of the cements (assuming that all the sulfate compound is dissolved). Composition of the cements: 1.6 g of  $\beta$ -TCP, 0.5 g of MCPM, x g of sulfate compound and 0.5 ml/g of deionized water (0.65 ml/g for CSH and 1.26 ml of sulfuric acid solution). The error bars correspond to a 90% confidence interval around the mean.

The solubility of the sulfate compounds in water are respectively: CSH:  $0.08 \text{ M}^9$ ; PS:  $0.7 \text{ M}^{10}$ ; MSHH:  $2.9 \text{ M}^{10}$ ; SSDH:  $2.9 \text{ M}^{10}$ . This order corresponds to the effectiveness of the sulfate compounds (fig. 2). Therefore, it seems that as soon as the solubility of the sulfate compound is reached, the setting time stays constant. This explains the difference of behavior observed between cements containing CSH and PS on one side, and MSHH and SSDH on the other side. However, these results do not give any explanation for the results obtained by Mirtchi et al.<sup>2</sup> who observed a tenfold increase of the setting time when adding 20% (weight) of CSH. Solubility calculations<sup>4</sup> have shown that the sulfate ions do not modify the solubility of calcium phosphates in the pH range of the beginning of the setting reaction (around  $\text{pH} = 3$ ). Moreover, sulfate ions decrease the growth rate of DCPD crystals<sup>4</sup>. Therefore, the first increase of the setting time has been attributed to the inhibitory effect of the sulfate ions on the growth rate of DCPD crystals.

Above a concentration of 0.1 M, the setting time decreases (fig. 2) and the microstructure of the cement becomes smaller and thinner (fig. 3 and 4). These phenomena are explained by the precipitation of calcium sulfate dihydrate (CSD;  $\text{CaSO}_4 \cdot 2\text{H}_2\text{O}$ ): first, the solubility of CSD lies around  $0.01 \text{ M}^4$ , i.e. way below 0.1 M. As the mixing liquid contains a large amount of calcium ions also, the solution is supersaturated versus CSD and should therefore precipitates CSD. Second, the crystallographic structure of CSD is nearly identical to that of DCPD<sup>11,12</sup>. Therefore, CSD crystals can act as heterogeneous nuclei for DCPD crystals and decrease

the size of the DCPD crystals. Finally, the precipitation of CSD consumes sulfate ions, which depletes their concentration in solution, and therefore lowers the setting time since sulfate ions decreases the growth rate of DCPD.

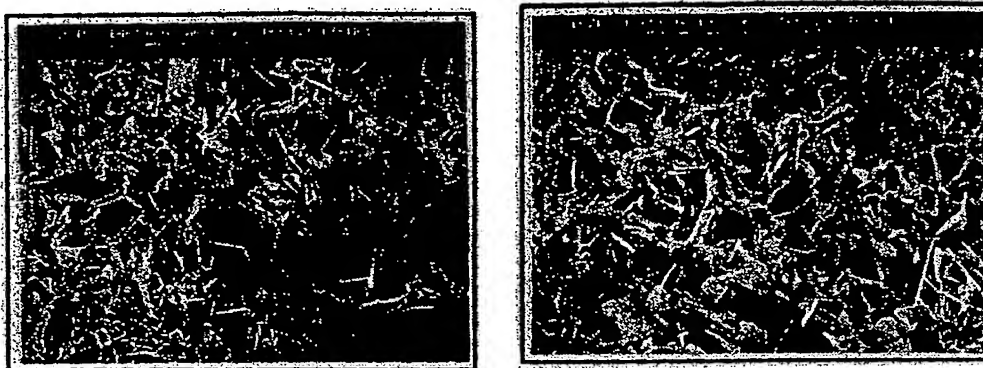


Fig. 3: Micrograph of a cement prepared with (a) 1.5 g of  $\beta$ -TCP, 0.6 g of MCPM, and 1.365 ml of deionized water, and (b) 1.5 g of  $\beta$ -TCP, 0.6 g of MCPM, 0.0875 g of CSH and 1.42 ml of deionized water.

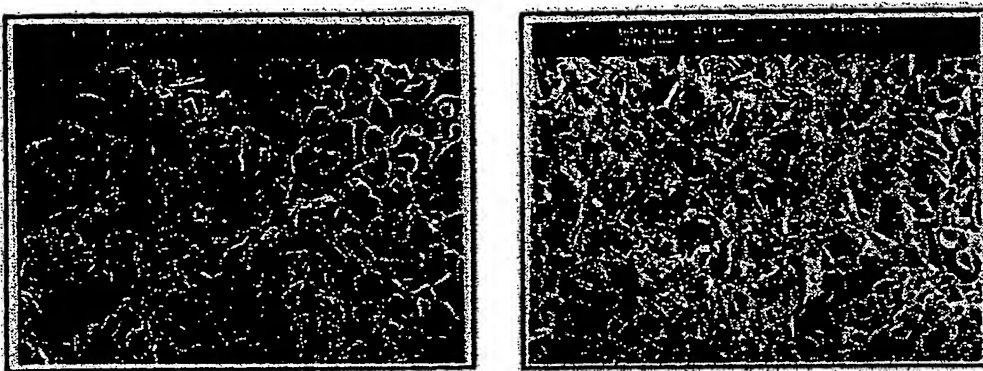
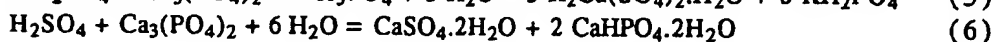
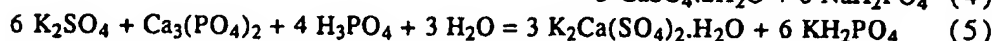
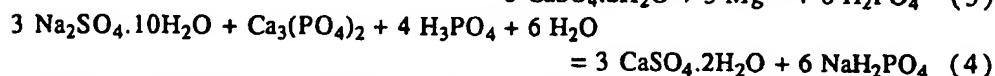
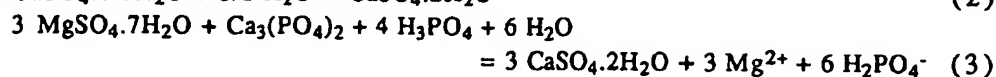
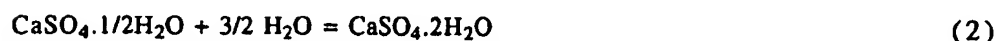


Fig. 4: Micrograph of a cement prepared with (a) 1.5 g of  $\beta$ -TCP, 0.6 g of MCPM, and 1.05 ml of deionized water, and (b) 1.5 g of  $\beta$ -TCP, 0.6 g of MCPM, 0.158 g of SSDH and 1.13 ml of deionized water.

The presence of CSD was detected by XRD in all the samples of cement except for those prepared with PS. The compositions determined by XRD are:

$\text{CaSO}_4 \cdot 1/2\text{H}_2\text{O}$	:	$\beta$ -TCP, DCPD, CSD
$\text{MgSO}_4 \cdot 7\text{H}_2\text{O}$	:	$\beta$ -TCP, DCPD, CSD + unknown compound
$\text{Na}_2\text{SO}_4 \cdot 10\text{H}_2\text{O}$	:	$\beta$ -TCP, DCPD, CSD, $\text{NaH}_2\text{PO}_4$
$\text{K}_2\text{SO}_4$	:	$\beta$ -TCP, DCPD, $\text{K}_2\text{Ca}(\text{SO}_4)_2 \cdot \text{H}_2\text{O}$ , $\text{KH}_2\text{PO}_4$
$\text{H}_2\text{SO}_4$	:	$\beta$ -TCP, DCPD, CSD

Therefore, the setting reactions leading to these compounds can be partly attributed to reaction (1) and partly to the following reactions:



These reactions show that except for  $\text{H}_2\text{SO}_4$  and CSH, all the other sulfate compounds consume phosphoric acid, and hence decrease the acidity of the mixing solution. As the solubility of CSD is very low compare to that of DCPD and as these two compounds are very similar, it can be assumed that equations (3) to (6) occur before equation (1). Therefore, if the amount of sulfate ions is large enough, the setting reaction expressed by equation (1) will not happen. This amount can be calculated for each sulfate compound assuming that 4 moles of  $\text{H}_3\text{PO}_4$  are equivalent to 3 moles of  $\text{Ca}(\text{H}_2\text{PO}_4)_2 \cdot \text{H}_2\text{O}$  (both have 8 hydronium ions):  $\text{MgSO}_4 \cdot 7\text{H}_2\text{O}$ : 1.28 M;  $\text{Na}_2\text{SO}_4 \cdot 10\text{H}_2\text{O}$ : 1.15 M;  $\text{K}_2\text{SO}_4$ : 0.81 M. These values are reasonably close to the sulfate ions concentration corresponding to the sharp increases of the setting time (fig. 2). Therefore, the second increase of the setting time is attributed to an excess of sulfate salts in the mixing solution. This effect should become more important as the weight fraction of the sulfate compound increases or the MCPM weight fraction decreases. This last result is evidenced on figure 5.

The effect of the sulfate concentration on the porosity of the cements is shown on figure 6. The porosity increases a lot when MSHH, SSDH and PS are added. These increases can be calculated using the initial and the final composition of the hardened cements and assuming (1) a constant apparent volume during the setting reaction and (2) that the setting reaction are given by equations (1) to (6). The correlation between calculated and measured porosities is good (fig. 7).



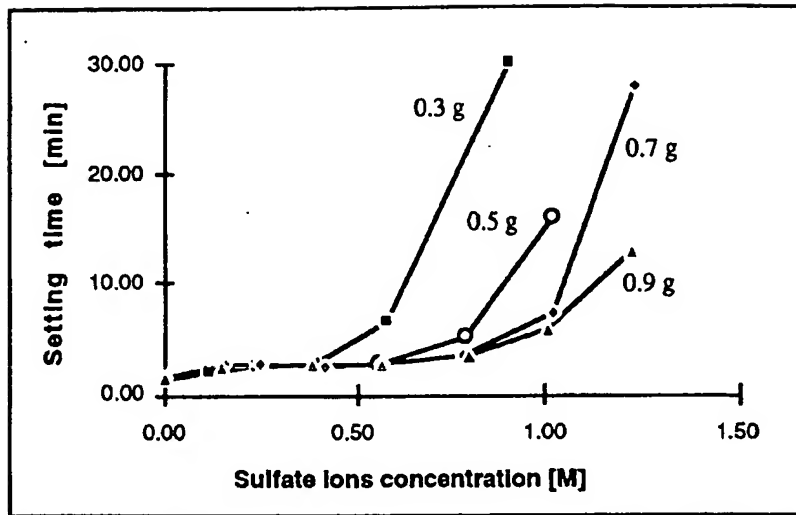
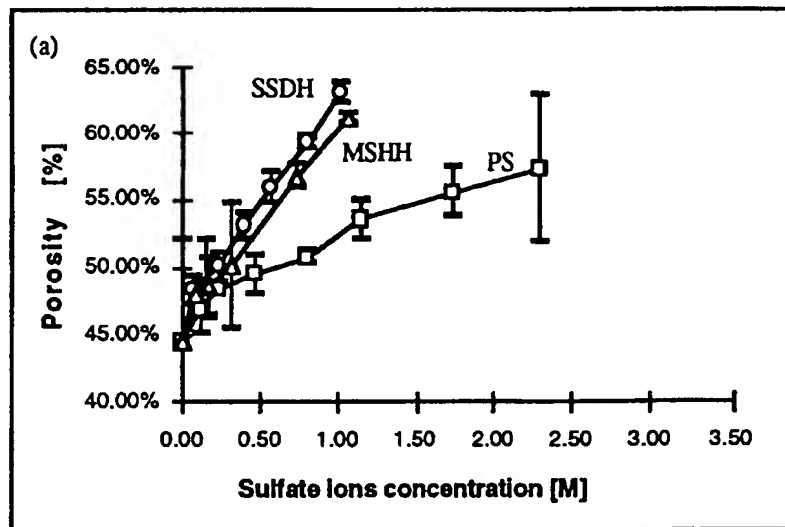


Fig. 5: Influence of the concentration of sulfate ions and the amount of MCPM on the setting time of the cements. Composition of the cements: 1.6 g of  $\beta$ -TCP,  $m_1$  g of MCPM ( $m_1 = 0.3, 0.5, 0.7$  and  $0.9$  g),  $m_2$  g of SSDH and 0.5 ml/g of deionized water. One measurement was performed for each point, except for 0.5 g of MCPM (2 measurements).



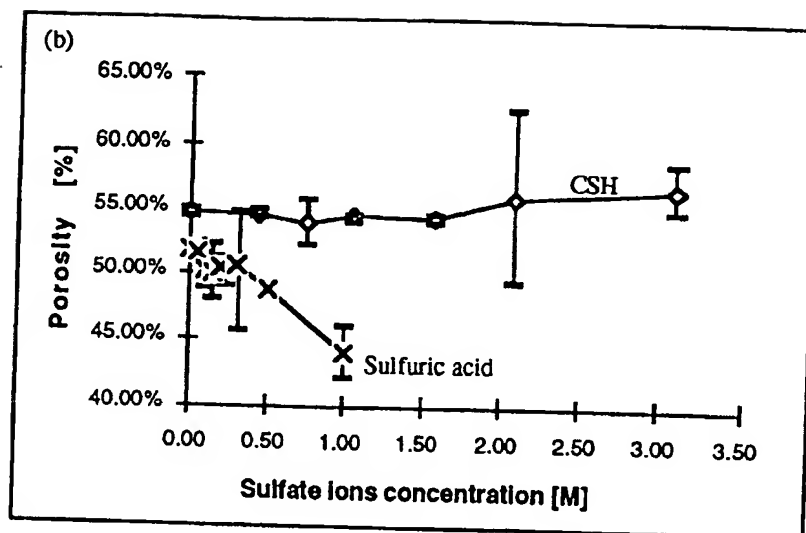


Fig. 6: Influence of the concentration of the sulfate ions on the porosity of the cements. Composition: 1.6 g of  $\beta$ -TCP, 0.5 g of MCPM, x g of  $\text{Na}_2\text{SO}_4 \cdot 10\text{H}_2\text{O}$  and 0.5 ml/g of deionized water (0.65 ml/g for CSH and 1.26 ml for sulfuric acid). The error bars correspond to a 90% confidence interval around the mean.

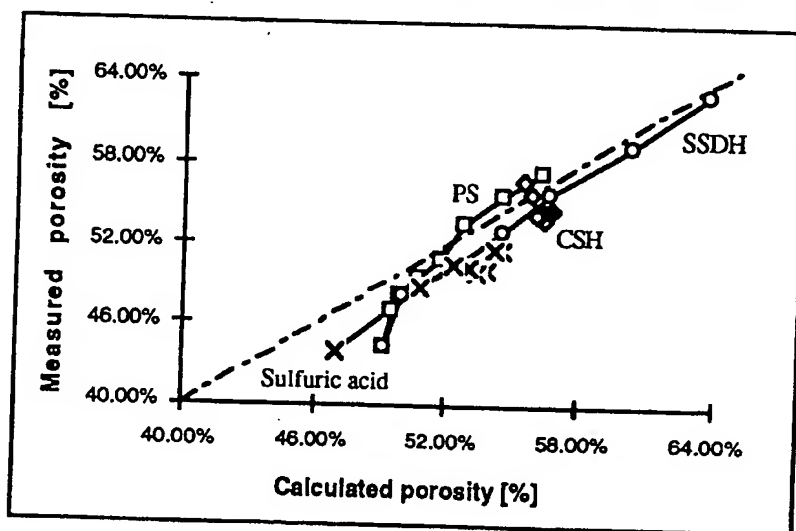


Fig. 7: Comparison between the measured and the calculated porosities. The dashed line correspond to "Measured porosity" = "Calculated porosity".

The tensile strength and the corrected tensile strength of the cements increase with increased amounts of sulfate ions until a maximum is reached (fig. 8 and 9). The maximum corresponds to the local minimum of the setting time (fig. 2). The increase of the tensile strength is due to the thinning of the microstructure. This is observed for all the sulfate

compounds, in particular for CSH (fig. 3) and SSDH (fig. 4). Above that point, the decrease of the tensile strength is probably due to the effect of reactions (2) to (6), which decrease the amount of binding phase (= DCPD).

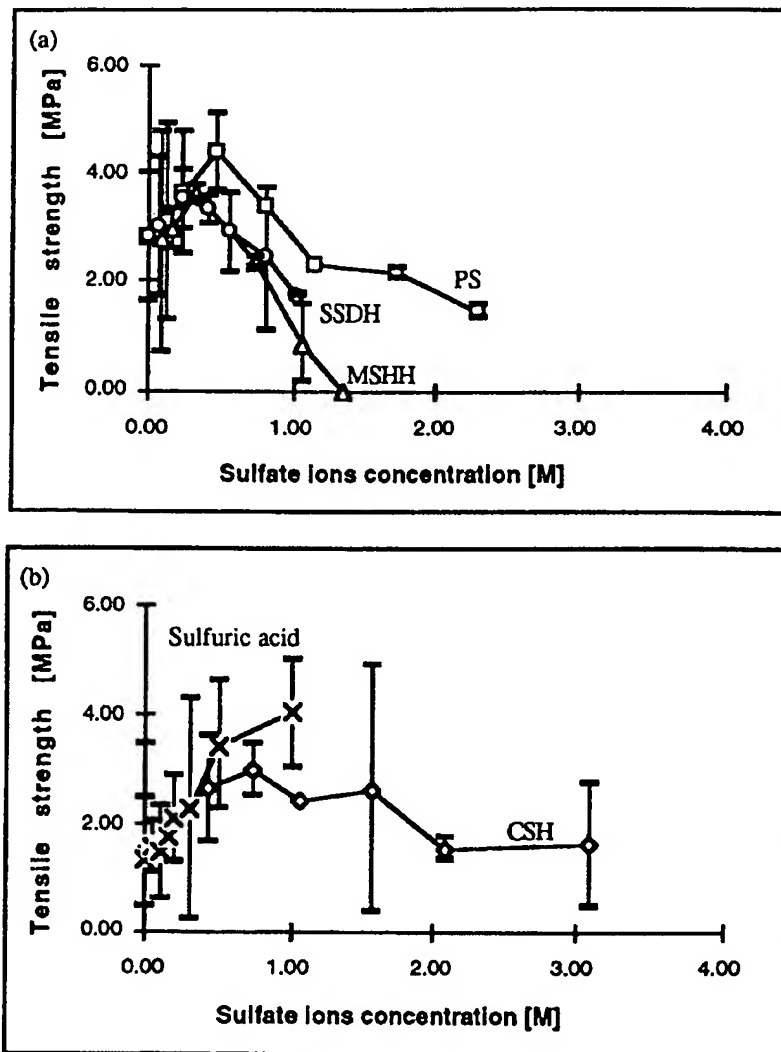


Fig. 8: Influence of the concentration of sulfate ions on the tensile strength of the cements. Composition: 1.6 g of  $\beta$ -TCP, 0.5 g of MCPM, x g of sulfate compound and 0.5 ml/g of deionized water (0.65 ml/g for CSH and 1.26 ml for sulfuric acid). The error bars correspond to a 90% confidence interval around the mean.

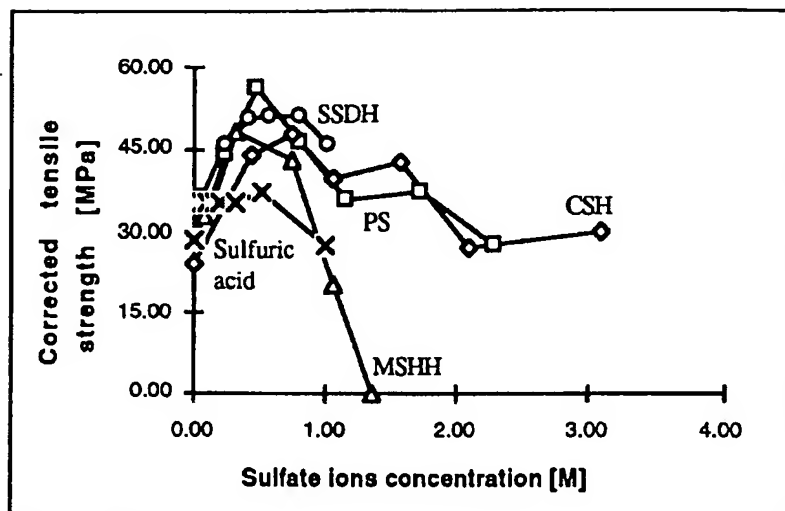


Fig. 9: Influence of the concentration of the sulfate ions on the corrected tensile strength of the cements. Composition: 1.6 g of  $\beta$ -TCP, 0.5 g of MCPM, x g of sulfate compound and 0.5 ml/g of deionized water (0.65 ml/g for CSH and 1.26 ml for sulfuric acid). The error bars were not put in order to keep the chart as clear as possible.

The figure 10 shows that the microstructure of the hardened cements is very heterogeneous. Considering its shape and its size, the defect represented on figure 10 is probably due to the dissolution of a MCPM crystal after the setting time. This effect damages the mechanical properties of the cement and explains why cements made of  $\beta$ -TCP/ $H_3PO_4$ / $H_2O$  mixtures have better properties than those made of  $\beta$ -TCP/MCPM/ $H_2O$  mixtures<sup>4</sup>.

Concerning the best way to add sulfate ions, the results show that among the various sulfate compounds considered in this study, sulfuric acid has the strongest effect on the local maximum of setting time (fig. 2) and the tensile strength (fig. 6). However, if a simultaneous long setting time and high tensile strength are desired, it is preferable to use MSHH, SSDH, or PS.

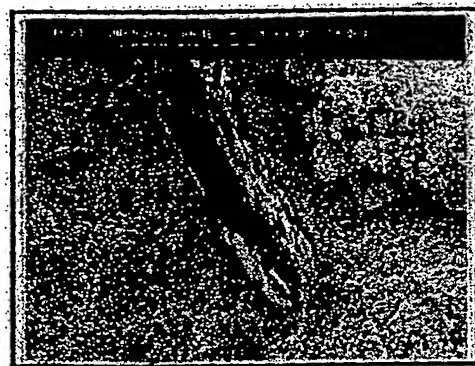
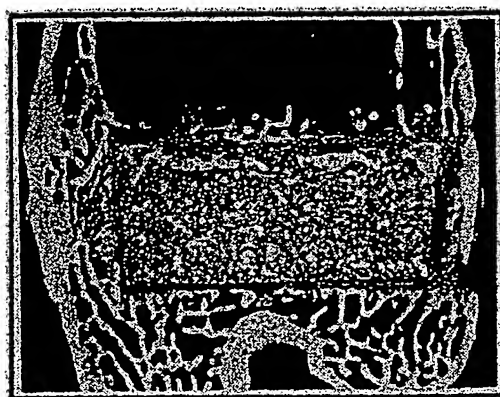


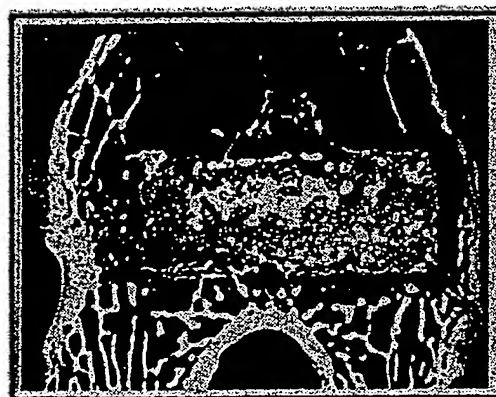
Fig. 10: Micrograph of a cement prepared with 1.5 g of  $\beta$ -TCP, 0.6 g of MCPM, and 1.05 ml of deionized water.

#### Preliminary *in vivo* results

Figures 11 show the evolution of the cement in the sites of implantation. After four weeks (fig. 11a), the cylinder of cement is surrounded by newly-formed bone (small trabeculae). After eight weeks, most of the cement has disappeared and been replaced by trabecular bone (fig. 11b). Finally, after sixteen weeks, the cement is totally replaced by trabecular bone (fig. 11c). In order to evaluate the real effect of the cement on the bone formation, the samples were compared with control samples, i.e. created cavities in the cancellous bone which were not filled with this type of cement. Figure 11d shows one of these samples: after 16 weeks, the cavity is still large and empty. These results mean that this type of cement is biodegradable, osteoconductive and therefore suitable as a bone substitute.



(a)



(b)



(c) (d)  
Fig. 11: Microradiograph of the samples of cement implanted in the distal femoral epiphyses of rabbits. (a) after 4 weeks; (b) after 8 weeks; (c) after 16 weeks; (d) control sample after 16 weeks. Scale: length of the samples of cement: 10 mm; diameter: 4.75 mm.

#### 4. Conclusion

The present study shows that sulfate ions can be used as a setting regulator for cements made of  $\beta$ -TCP - MCPM - water mixtures. This result is in accordance with that of Mirtchi et al<sup>2</sup>, except a tenfold increase of the setting time was not observed.

Except for CSH and sulfuric acid, two sharp increases of the setting time were observed. The first, which occurs below a sulfate ions concentration of around 0.1 M, is attributed to the inhibitory effect of sulfate ions on the growth rate of DCPD crystals. Above that concentration, CSD precipitates and acts as a heterogeneous nuclei for the growth of DCPD. This leads to a decrease of the setting time. As the concentration of sulfate ions is further increased, the second sharp increase of the setting time occurs at around 0.9 M. This is due to the consumption of MCPM by the sulfate compounds which limits the formation of the binding phase (DCPD) and therefore decreases the tensile strength of the cements. The consumption of MCPM does not happen with sulfuric acid. Therefore, only the first increase of the setting time is observed. In the case of CSH, there is a slow but steady increase of the setting time with increasing amounts. This is attributed to the low solubility of CSH, which prevents a high concentration of sulfate ions in the mixing liquid.

The porosity of the cements can be calculated using the initial and the final composition of the hardened cements and assuming that the apparent volume of the cement is constant during the setting reactions given by equations (1) to (6). The correlation between calculated and measured porosities is good.

The tensile strength of the cements reaches a maximum at a sulfate ions concentration of around 0.5 M. This concentration corresponds to the local minimum of the setting time for PS, SSDH and MSHH. The maximum is due to the combined effect of a decrease of the size of the DCPD crystals (increase of the strength) and a decrease of the amount of DCPD in the hardened cement (decrease of the strength).

The *in vivo* results show that the cement made of 64%  $\beta$ -TCP, 20% MCPM, 16% CSH is nearly totally resorbed and replaced by new bone after 8 weeks, in contrast to zero bone growth in 16 weeks without the cement. This means that this type of cement is biodegradable, osteoconductive and therefore suitable as a bone substitute material.

### Acknowledgements

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### References

- <sup>1</sup>A.A. Mirtchi, J. Lemaître, N. Terao, "Calcium phosphate cements: study of the  $\beta$ -tricalcium phosphate-monocalcium phosphate system", *Biomaterials*, 10 [september] 475-480 (1989).
- <sup>2</sup>A.A. Mirtchi, J. Lemaître, E. Munting, "Calcium phosphate cements: action of setting regulators on the properties of the  $\beta$ -tricalcium phosphate-monocalcium phosphate cements", *Biomaterials*, 10 [november] 634-638 (1989).
- <sup>3</sup>A.A. Mirtchi, J. Lemaître, E. Munting, "Microstructure and strength development in calcium phosphate biocements", *Advanced Materials and Processes*, 2 797-802 (1990).
- <sup>4</sup>M. Böhner, "Propriétés physico-chimiques et ostéogéniques d'un biociment hydraulique à base de phosphates de calcium", PhD Thesis N°1171, Swiss Federal Institute of Technology (EPFL), Lausanne, Switzerland, 1993.
- <sup>5</sup>E. Munting, A.A. Mirtchi, J. Lemaître, "Bone repair of defects filled with a phosphocalcic hydraulic cement: an *in vivo* study", *Journal of Materials Science: Materials in Medicine*, 4 337-344 (1993).
- <sup>6</sup>M. Böhner, J. Lemaître, J. Cordey, S. Gogolewski, T.A. Ring, S.M. Perren, "Potential use of biodegradable bone cement in bone surgery: holding strength of screws in reinforced osteoporotic bone", *Orthopaedic Transactions*, 16[2] 401-402 (1992).
- <sup>7</sup>L.L. Hench, J. Wilson, "Bioceramics", *MRS Bulletin*, September 62-74 (1991).
- <sup>8</sup>M. Böhner, J. Lemaître, T.A. Ring, "Hydraulic properties of tricalcium phosphate - phosphoric acid - water mixtures", *Third Euro-Ceramics Proceedings*, 3 95-100 (1993).
- <sup>9</sup>Klepetsanis P.G., Koutsoukos P.G., "Spontaneous precipitation of calcium sulfate at conditions of sustained supersaturation", *Journal of Colloid and Interface Science*, 143 299-308 (1991).

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<sup>10</sup>Handbook of Chemistry and Physics, 64th Edition, CRC Press, 1983-1984.  
<sup>11</sup>Beevers C.A., "The Crystal Structure of Dicalcium Phosphate Dihydrate, CaHPO<sub>4</sub>·2H<sub>2</sub>O", Acta Cryst., 11, 273-277, 1958.  
<sup>12</sup>Sakae T., Nagata H., Sudo T., "The crystal structure of synthetic calcium phosphate-sulfate hydrate and its relation to brushite and gypsum", American Mineralogist, 63, 520-527, 1978.